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PREPs and conventional products, and suitable contrast groups. Concomitant, coordinated toxicological studies should be performed to provide biological correlations with clinical outcomes. Such outcomes as fetal birthweight and incidence of other reproductive and developmental health outcomes (e.g., fertility outcomes, placental complications, gestational age at birth, incidence of SIDS, spontaneous abortion etc.) should be considered primary objects of study.

Findings in pregnant women exposed to PREPs may have value beyond maternal/fetal outcomes. The nature of adverse effects from PREP exposure will likely be determined much sooner in pregnant women (several months) than findings on chronic disease outcomes such as various cancers and cardiovascular disease in nonpregnant tobacco users. Should adverse findings become apparent, there may substantial implications for risk of chronic illnesses among nonpregnant adults, and coordinated pathogenic studies might allow conclusions on new tobacco product outcomes in advance of studies exploring longer "incubation periods."

### Studies on the Component Exposures of PREPs

The committee recommends that further basic research be undertaken to elucidate the components of cigarette smoke that are primarily responsible for adverse health outcomes. In order to evaluate the safety of many PREPs, it is important to understand the effect of smoke components, especially nicotine and CO, on the pathogenesis of intrauterine growth retardation, spontaneous abortions and other health outcomes. In addition, better understanding of the risks of bupropion SR use by pregnant women (i.e., seizure risk) and the teratogenic effects of nicotine on the central nervous system, including dose-response and periods of vulnerability during gestation, is needed for adequate risk–benefit analysis of the harm reduction potential of these products.

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growth retardation through increased tissue hypoxia. Nicotine has also been thought play a role through increasing vasoconstriction and decreasing perfusion through the placenta.

Although nicotine replacement products and bupropion SR are currently not approved by the Food and Drug Administration for use by pregnant women, the Agency for Healthcare Research and Quality's (AHCRQ) Clinical Practice Guidelines for Treating Tobacco Use and Dependence (Fiore et al., 2000) recommend that "Pharmacotherapy should be considered when a pregnant woman is otherwise unable to quit, and when the likelihood of quitting, with its potential benefits, outweighs the risks of the pharmacotherapy and potential continued smoking". It is generally thought that NRT can reasonably be used with pregnant patients if prior behavioral modifications have failed and the patient continues smoke at least 10–15 cigarettes per day (ACOG, 1997). There are no data regarding the efficacy of potential reduced-exposure products (PREPs) during pregnancy, but there is the presumption that the tobacco-related PREPs are likely to have toxic effects at some level and that, until further evidence is produced, existing guidelines concerning pharmacological PREPs still pertain.

## RECOMMENDATIONS

### Surveillance of Tobacco Use Patterns Among Pregnant Women

Central to understanding exposure to tobacco products is continuous population information on patterns of tobacco use among pregnant women. This may not be attainable by general population survey methods, due to inadequate sample sizes and insufficient representation of various geographic or demographic groups or of the earliest stages of pregnancy. Thus, surveys should be devoted specifically to pregnant women in all stages of gestation, irrespective of receipt of medical care. Survey content should include other known or putative causes of adverse maternal or fetal outcomes, as well as detailed product types and usage patterns as delineated in Chapter 6, in recommendations for general population surveillance.

Biochemical and toxicological exposure measures should be a routine part of surveillance for exposure to conventional products as well as PREPs. These will be necessary to conduct more precise, coordinated toxicological studies and also to assess actual exposure rates more accurately. For example, dose may be measured by maternal serum and urine cotinine levels, which have shown reliable correlations with maternal and consequently fetal tobacco smoke exposure. Self-reported smoking data can be unreliable, since pregnant women who have been advised to quit tend to under report tobacco use because of the stigma attached to smoking (Kendrick et al., 1995). Also, self-reports do not adequately account for differences in depth and frequency of puffs among smokers.

### Assessment of Fetal and Maternal Outcomes Associated With New Tobacco Product Exposure

To practically assess the health effects of PREPs, reliable measures of health outcomes that can be utilized in a relatively short time are desired. Among the reproductive outcomes of maternal smoking, intrauterine growth retardation resulting in low birthweight babies has been extensively studied, and a large body of evidence has supported a causal link with cigarette smoke exposure. The committee recommends, based on currently available scientific knowledge, that fetal birthweight and intrauterine growth retardation be used as the outcome measure in evaluating the harm reduction potential of the use of PREPs. Study designs might include repeated cohort or case-control studies of pregnant women with an appropriate distribution of exposures to both

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were diminished when measured within days of birth after in utero smoke exposure. This study also found an effect on volume measurements and a dose–response relationship to number of cigarettes smoked per day. A study of infants who were 7 weeks premature (Hoo et al., 1998) suggests that the detrimental effects on respiratory function occur before the last trimester and further supports the predominant effects of in utero smoke exposure compared to postnatal ETS exposure.

Suggested mechanisms of airway dysfunction caused by cigarette smoke exposure during pregnancy include decreased airway compliance, poor bronchial tree development, and emphysema-like changes of the alveoli (Lodrup Carlsen et al., 1997, Cunningham et al., 1994). Several animal studies have shown impaired fetal lung growth, including decreased lung interstitium and elastic tissue (Moessinger, 1989; Maritz et al., 1993). It has been suggested that nicotine interferes with the synthesis of elastic tissue needed for stability of the alveoli and that other smoke constituents may promote protease function (Maritz et al., 1993). See Chapter 14 for further discussion of this topic.

## SMOKELESS TOBACCO

Reproductive effects of smokeless tobacco have been less extensively studied than those of smoking. Many of the human data come from countries in which consumption of tobacco in other forms is more widespread among women. Animal studies have shown significant weight reduction and perinatal mortality among rat fetuses of mothers exposed to smokeless tobacco, administered through gastric intubation of smokeless tobacco aqueous extract (Krishna, 1978; Paulson et al., 1994). Researchers in India have found a significant decrease in birthweight of infants born to mothers who use smokeless tobacco (Krishnamurthy and Joshi, 1993; Deshmukh et al.,1998; Verma et al., 1983). Changes in placental anatomy were also noted by Agrawal and colleagues (1983), who discovered the placenta of tobacco-chewing mothers to be on average 65.9 grams heavier than that of non-using mothers. It has been suggested that nicotine-induced vasoconstriction and decreased perfusion may be the primary mechanism leading to decreased fetal growth in mothers who use smokeless tobacco (Verma et al., 1983).

## CONCLUSIONS

Exposure to cigarette smoking is a major cause of fetal and infant morbidity and mortality. This is particularly true for the association with low birthweight and it consequences, as well as for preterm delivery and SIDs. For several important adverse reproductive effects of maternal smoking, a decrease in smoking has been found to decrease or be associated with a decrease in risks to the fetus and infant. The greatest benefit, of course, comes from smoking cessation. However, many women continue to smoke during pregnancy, despite knowledge of the harmful effects of smoking and personal experience with adverse fetal and infant conditions. Moreover, as current rates of smoking among adolescent women slowly rise, these adverse effects associated with tobacco smoke exposure while pregnant may worsen.

On average, infants exposed to maternal smoking in utero are 200 grams lighter and 1.4 cm shorter than those who are unexposed. A strong dose–response has been supported in numerous studies and a decrease in dose (number of cigarettes) in controlled studies has led to increased birthweights in a predictable pattern. What is known about the mechanism of effect of cigarette smoke on the fetus suggests a multifactorial etiology, with CO considered to play a major role in

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effect. This study found an overall 55% increase in the risk of infant CLP among all pregnant smokers, with the risk almost 80% higher for women who smoked more than a pack a compared to nonsmoking mothers (Chung, 2000). Results have also been inconsistent regarding the interaction of maternal smoking with the rare transforming growth factor-α (TGF-α) allele and association with CLP (Chistiansen et al., 1999).

## COGNITIVE AND BEHAVIORAL DEFICITS IN CHILDHOOD

Tobacco use during pregnancy has been linked to neurological damage that may be expressed during childhood as intellectual deficits, behavioral problems, and poor school achievement. Studies have found significant differences in IQ scores and increased likelihood of mental retardation in children of mothers who smoked during pregnancy compared to children of nonsmokers (Olds et al., 1994; Drews et al., 1996). The differences are decreased but generally persist after control for environmental and parental factors that may influence intelligence. Attention deficit hyperactivity disorder (ADHD) has been associated with smoking during pregnancy. An OR of 2.7 has been found for the risk of children of mothers who smoked during pregnancy after controlling for socioeconomic status, parental ADHD, and parental IQ. Furthermore, conduct disorder and disruptive behavior have been found to have a weak dose-related association with maternal cigarette smoking after control for confounding social factors (Fergusson et al., 1993).

Postulated mechanisms of cognitive impairment involve effects of cigarette smoking on the fetus including chronic hypoxia, decreased nutrition, and direct toxicity to cortical tissue by toxins such as CO, nicotine, and lead in cigarette smoke. Small-for-gestational-age infants, a significant adverse effect of maternal cigarette smoking as discussed previously, have been independently linked in several studies to decreased cognitive abilities (measured by IQ scores) into childhood and adolescence, compared to children of normal birthweight (McCarton et al., 1996; Sommerfelt et al., 2000; Seidman et al., 1992). Animal models have linked fetal nicotine exposure to upregulation of nicotinic receptors causing hyperactivity in infant mice (Milberger et al., 1996). Also, fetal nicotine exposure has potentially detrimental effects on fetal brain development through premature stimulation of nicotinic cholinergic receptors in the fetal brain causing disruption of the development of cholinergic neurons, which affects numerous other neurotransmitters and hormones, including catecholamines, serotonin, and dopamine (Benowitz et al., 2000).

## FETAL LUNG DEVELOPMENT

Maternal smoking during pregnancy has been demonstrated to be associated with abnormal effects on fetal lung function and development, possibly contributing to increased incidence of early childhood respiratory diseases, including bronchitis, pneumonia, and asthma (Morgan and Martinez, 1998; Joad, 2000). Based on a review by Joad (2000), in utero cigarette smoke exposure more than doubles the risk for disease of airway hyperresponsiveness in childhood, including wheezing illnesses and asthma. In a large cross-sectional study, Cunningham and colleagues (1994) found significantly lower measures of flow in pulmonary function tests among 8–12 year olds who were exposed to maternal smoking compared to children of nonsmokers. After controlling for prenatal exposure, no significant effect of current ETS exposure was found. This finding was further supported in a study by Tager et al. (1995) that found significantly lower expiratory flow measurements of infants up to 18 months of age among mothers who smoked during pregnancy. Lodrup Carlsen and colleagues (1997) found supporting evidence that flow parameters

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have been reliable markers of maternal nicotine intake and cigarette use and useful tools in predicting infant birthweight (Haddow et al., 1987; Li et al., 1993). Cotinine levels in infant cord blood are highly correlated with maternal serum and urine cotinine concentrations, r =. 91 and r = .72, respectively (Wang et al., 1997). Among African-Americans, a few studies have noted differences in the relationship between cigarette consumption and cotinine concentrations. Specifically, these studies have shown higher cotinine levels for all cigarette dose levels among African-Americans (English et al., 1994). This group also reported no significant difference in birthweight reduction per 1 ng/ml maternal cotinine among black infants compared to white infants, and Li et al. (1993) found that among mothers with high baseline cotinine levels (>200 ng/ml), the birthweights of black infants were less sensitive to smoking reduction than those of white infants.

The pathogenesis of low birthweight secondary to smoking is not known but is generally thought to be multifactorial. The probable mechanisms involved include CO formation of carboxyhemoglobin in maternal and fetal circulation, causing decrease in oxygen delivery and resulting in tissue hypoxia and increased viscosity that may affect placental perfusion (Benowitz et al., 2000). Cyanide in tobacco smoke can decrease stores of vitamin $B_{12}$, a cofactor for fetal growth (Ness et al., 1999); Additionally, smoking-related maternal and fetal nutritional deficits caused by cigarette smoking have been postulated as mechanisms for fetal growth retardation. Reduction in uteroplacental blood flow due to the vasoconstrictive catecholamine-mediated effects of nicotine has been suggested as a possible mechanism of intrauterine growth retardation and has been studied in animal models (Bassi et al., 1984). These findings have not been fully supported by measurements of placental blood flow in humans (Benowitz et al., 2000).

## SUDDEN INFANT DEATH SYNDROME (SIDS)

It is estimated that more than 50% of the risk of SIDS may be attributed to exposure to cigarette smoke (Dwyer et al., 1999). A positive association between maternal smoking and SIDS has been consistently supported in the literature (reviewed in Golding, 1997; Leach et al., 1999). Generally, the risk of SIDS increases two- to fourfold among infants of mothers who smoke during pregnancy, and the risks increase even further when combined with postnatal exposure to tobacco smoke (ACOG, 1997). However, it has been difficult to separate the effects of postnatal smoke exposure from the effects of prenatal tobacco smoke exposure (Golding, 1997; Spiers, 1999). A recent prospective study found an OR of 2–3 for the association between prenatal maternal smoking and risk of SIDS, and an OR of roughly 3 for postnatal maternal smoking; however, no significant effect was seen for smoke exposure from other household members or maternal smoking restricted to rooms without the infant (Dwyer et al., 1999). The mechanism of effect is not fully known. It has been suggested, based on animal models, that fetal nicotine exposure results in loss of the normal response of the adrenomedullary system to hypoxia (Benowitz, 1998; Slotkin et al., 1995, 1997). Furthermore, the increased susceptibility of infants of smoking mothers to respiratory infections may play a role.

## CONGENITAL MALFORMATIONS

Oral clefts is the most extensively studied malformation thought to be associated with maternal smoking. Research has failed to show a consistent association, although a moderate association with cleft lip ± cleft palate (CLP) has been described (Lieff et al., 1999). A recent study found a strong positive association between cigarette smoking and CLP, with a dose–response

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An earlier prospective interventional trial by Li (1993) found no improvement of gestational age with smoking reduction but did show a significant improvement after smoking cessation.

The mechanism of smoke-attributed preterm delivery is not certain but may be related to intrauterine infections secondary to decreased immunity, structural abnormalities especially the loss of integrity of type III collagen, or the increase in production of prostaglandin ($PGE_2$), causing myometrial muscle contractions (Cnattigius et al., 1999).

## LOW BIRTHWEIGHT

The detrimental effect of smoking on birthweight has been extensively studied and well documented. This effect has been labeled "fetal tobacco syndrome," which is described as maternal smoking of five or more cigarettes per day during pregnancy, no evidence of maternal hypertension during pregnancy, symmetrical growth retardation of newborn at term, and no other explicit cause of intrauterine growth retardation (Benowitz, 1991; Nieburg et al., 1985). Twelve percent of infants born to all mothers who are smokers weighed less than 2,500 grams (low birthweight) in 1998, and eleven percent of infants born to mothers who report smoking as few as one to five cigarettes per day have low birthweight (CDC, 2000). Among pregnant smokers the risk of low birthweight babies is doubled compared to nonsmokers, and about 20% of all low birthweight babies are attributable to smoking (U.S. DHHS, 1983). Infants born to mothers who smoke during pregnancy are on average 200 grams lighter and 1.4 cm shorter than infants of nonsmokers (Wang et al., 1997). The effect of smoking is particularly prominent if exposure occurs after the first trimester. The association persists even after controlling for confounding factors such as maternal age, maternal nutrition, socioeconomic level, education, maternal weight gain, and alcohol consumption (reviewed in ACOG, 1997). Long-term effects of maternal smoking on growth have not been described, but small-for-gestational-age infants have a higher incidence of certain illnesses and disabilities into childhood and adulthood, such as cardiovascular disease, non-insulin-dependent diabetes mellitus, and hypertension (reviewed in Barker, 1997, 1999; Forsen et al., 2000).

Environmental tobacco smoke has also been suggested to have a significant association with intrauterine growth retardation. A recent Swedish study found an OR of 2.4 for low birthweight infants among nonsmoking mothers exposed to ETS and an OR of 3.6 for smoking mothers exposed to ETS (Dejin-Karlsson et al., 1998). Paternal smoking has also been shown to have an adverse effect on infant birthweight. Martinez et al. (1994) report an 88-gram average reduction in birthweight of infants whose fathers smoked more than 20 cigarettes per day.

The dose–response evidence has been studied, extensively, and the findings suggest reversibility of risk with smoking reduction (Li et al., 1993; Sexton and Hebel, 1984; Hebel et al., 1988; Ahlsten et al., 1993). Li and his colleagues (1993) in a prospective intervention trial found that reduction as well as cessation of smoking (defined by serum cotinine levels) resulted in significantly increased birthweights compared to women who continued to smoke. Secker-Walker et al. (1998) reported that women who stop smoking before 20 weeks' gestation obtain maximum benefits of smoking reduction. Others have found that cessation even late in pregnancy led to normal-weight infants (Hebel et al., 1988; Ahlsten et al., 1993). Attempts have been made to quantify the relationship of cigarette consumption and fetal growth outcomes. One such study, which evaluated taking the average of serial cotinine measurements over the entire pregnancy, reported that for every 1,000-ng/ml increase in urine cotinine concentration, there was an associated 59 ± 9 gram reduction in birthweight, a ≅ 0.25-cm reduction in length, and a ≅ 0.12cm reduction in head circumference (Wang et al., 1997). Maternal serum and urine cotinine levels

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## PLACENTAL COMPLICATIONS

Findings have been consistent regarding the positive association of smoking with placenta previa (obstruction of the internal cervical os by the placenta), with a relative risk (RR) = 1.3–2.6 and placental abruption (premature separation of the placenta from the uterus), RR = 1.4–1.6 (reviewed in Castles et al., 1999; Andres and Day, 2000). These pregnancy complications cause at least one-fifth of all prenatal deaths (Ananth et al., 1996). Also, among smokers the perinatal death rate after placental abruption is two to three times higher than among nonsmokers (Werler, 1997). There has been consistent evidence that smoking is an independent risk factor for placenta previa and placental abruption after control for potential confounders including maternal age and parity, hypertension, preeclampsia, and alcohol use.

Studies have suggested a dose-dependent association between reported numbers of cigarettes smoked and placental complications, but the data have been inconclusive (Ananth et al., 1996; Handler et al., 1994; reviewed in Andres, 1996). Although the exact mechanism by which maternal smoking causes placental complications is unknown, the placentas of smokers exhibit anatomical and histological changes that suggest hypoxia and underperfusion (Voigt et al., 1990). The placentas of smokers have been found to be larger and heavier than those of nonsmokers (Christianson, 1979; Pfarrer et al., 1999). Pfarrer et al. (1999) found increased angiogenesis within the placental villi of smokers, thought to be a response to hypoxic stress caused by the components of cigarette smoke. Pfarrer and colleagues speculated that this adaptive response contributes to the large placentas of maternal smokers. Histologic studies have found necrotic and hemorrhagic changes of the decidua basalis, including calcification, hypertrophy, and thickening of the basement membrane (reviewed in Voigt et al., 1990). The hypoxic and ischemic changes in placental tissues are possibly due to damage of the endothelial cells of placental vessels resulting in decreased tissue perfusion and to the increase in carboxyhemoglobin resulting in decreased oxygen delivery (Ananth et al., 1996). It has also been postulated that smokers are more prone to placental inflammation and infection secondary to a smoking-related decreased immune response.

## PRETERM DELIVERY

Preterm delivery is defined as delivery before 37 weeks gestation and is an important cause of perinatal mortality. Studies have suggested an increase in the risk of preterm delivery among maternal smokers but have been inconsistent regarding the magnitude of risk (20% to >100% increased risk). Evidence of a dose–response association has been demonstrated (Shiono et al., 1986; Cnattingius, et al., 1999, reviewed in Shah and Bracken, 2000). Risk of infant mortality was more pronounced for very preterm births for preterm delivery (≤32 weeks gestation) (Windham et al., 2000; Kyrklund-Blomberg and Cnattingius, 1998) and with spontaneous versus induced preterm births after controlling for complications of pregnancy such as placental abruption, placenta previa, premature rupture of membranes, and hypertension (Kyrklund-Blomberg and Cnattingius, 1998).

The literature has supported the reduction of risk of preterm delivery associated with smoking cessation. A large population-based cohort study of Swedish women by Cnattingius et al. (1999) found that among nonsmokers with a term first delivery, those who initiated smoking after the first pregnancy had a greater risk of subsequent preterm pregnancies compared to women who did not smoke during pregnancy. Maternal smokers with an initial term delivery reduced their risk of subsequent preterm deliveries by stopping smoking prior to the second pregnancy.

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to threefold among smokers (Werler, 1997). Consistent with many previous studies, a recent cohort study of current and past smokers during assisted reproduction cycles suggested a dose-related decrease in ovarian function and a 50% reduction in pregnancy rates of current smokers (Van Voorhis et al., 1996). Also, a positive relationship (odds ratio, OR ≅ 1.3–2.2) between cigarette smoke exposure at conception and during pregnancy and the risk of subsequent ectopic pregnancy has been documented, with mixed results regarding dose–response (Coste et al., 1991; Handler et al., 1989; Stergachis et al., 1991; Saraiya et al., 1998). Animal studies have suggested altered gonadotropin release, decrease in luteinizing hormone (LH) surge, inhibition of prolactin release, altered tubal motility, and impairment of blastocyst formation and implantation as possible mechanisms of fertility impairment among smokers (reviewed in Hughes and Brennan, 1996). Additional studies in rats have shown follicle destruction and oocyte depletion when exposed to benzo[a]pyrene (BaP), a tobacco smoke toxin (Cooper et al., 1999). Furthermore, an evaluation of the Women's Health Study found that current and former smokers, after adjusting for age, race, education, marital status, number of sexual partners, frequency of intercourse, history of gonorrhea, and current method of contraception, had a significantly increased risk of pelvic inflammatory disease, possibly related to impairment of immunity and altered tubal factors (Marchbanks et al., 1990; Scholes et al., 1992). Pelvic inflammatory disease is an independent risk factor for ectopic pregnancy and infertility.

The association of altered male fertility with cigarette smoking is less consistent. Studies have shown mixed results with respect to sperm and semen quality and have not supported detrimental effects on male fertility (reviewed in Hughes and Brennan, 1996). Several animal and human studies have established an increased risk of vascular erectile dysfunction associated with cigarette smoking (U.S. DHHS, 1990; Juenemann et al., 1987; Shabsigh et al., 1991), including a large survey of Vietnam-era veterans, age 31 to 49, which found a 50% increase in the risk of impotence in smokers after controlling for all other major risk factors for impotence (Mannino et al., 1994).

## SPONTANEOUS ABORTIONS

Numerous studies suggest a positive, dose-related association between smoking and spontaneous abortions, with the risk reported to be increased 20–80% (Kline et al., 1977, 1983; Ness et al., 1999). A prospective study by Ness et al. (1999) of adolescent girls and women that presented to an emergency room found a strong correlation between the risk of spontaneous abortion and the presence of cotinine (threshold concentration = 500 ng/ml) in the urine (OR = 1.8). The association is found primarily in the second trimester and for chromosomally normal spontaneous abortions (Kline et al., 1995) thought to be associated with intrauterine growth retardation. Postulated causal mechanisms include fetal hypoxia mediated by carbon monoxide (CO) and placental and uterine vascular insufficiency or teratogenic effects mediated by nicotine (Ness et al., 1999; Kline et al., 1995). The effect is modified by alcohol consumption, caffeine use, and history of previous spontaneous abortions (Ness et al., 1999; Windham et al., 1992). Although recent large prospective study found no consistent evidence of an association between environmental tobacco smoke and spontaneous abortion (Windham et al., 1999), a few earlier studies have described such a relationship (Windham et al., 1992; Chatenoud et al., 1998; Ahlborg and Bodin, 1991).

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# Reproductive and Developmental Effects

Smoking among women of reproductive age is a critical risk factor for reproductive health problems including fetal and infant mortality and impaired fetal development. Cigarette smoking has numerous well-documented adverse effects on pregnancy and fetal health, including low birthweight, preterm delivery, perinatal morbidity, placental complications, and increased risk of sudden infant death syndrome (USDHHS, 1988 and 1990). The harmful effects of cigarette smoke exposure during pregnancy have been well known for decades; nevertheless, a significant fraction of pregnant women continue to smoke and smoking continues to account for an estimated 10% of all fetal mortality (Kleinman et al., 1988). The percentage of women who smoke during pregnancy declined from 13.6% in 1996 to 12.9% in 1998 with rates being highest for non-Hispanic whites, American Indian, and Hawaiian women and for women of lower socioeconomic and educational levels (CDC, 1998, 1999, 2000). The number of cigarettes smoked per day has also steadily declined over the last decade with about a third of maternal smokers reporting smoking at least a half a pack per day in 1996 compared to more than 40% in 1990 (CDC, 1998). Among pregnant teenagers, however, the smoking rate increased from 18.8% in 1997 to 19.2% in 1998 (CDC, 2000).

Trends in maternal smoking behavior, based on data from the Behavioral Risk Factor Surveillance System, showed a decline in overall smoking initiation among women aged 18–44 to a reported rate of 38.2% in 1996, with no difference between pregnant and nonpregnant women. Reported rates of quitting in the same population have shown little change among pregnant and nonpregnant women, 25.2% and 14.4%, respectively in 1996, (Ebrahim et al., 2000). Even after learning that they are pregnant, 54% of women continue to smoke (Ebrahim et al., 2000). Additionally, maternal smokers who have experienced previous preterm delivery or small-for-gestational age infants do not show greater quit rates than smokers who have had uncomplicated deliveries (Cnattigius et al., 1999). According to the National Health Interview Survey (1992–1993), among female smokers in general, 72.5% reported that they wanted to quit smoking with 34% attempting to quit each year and 2.5% being successful.

The contribution of environmental tobacco smoke (ETS), including paternal smoking, to adverse reproductive health outcomes is uncertain, but ETS exposure is widespread among women of reproductive age. Data from the third National Health and Nutrition Examination Survey report a 32.9% prevalence of ETS exposure at home or at work among non-tobacco-using females age 17 and over.

## FERTILITY IMPAIRMENT

Smoking has been associated with increased time to conception, decreased pregnancy rate in assisted reproduction, increased risk of ectopic pregnancy, and menstrual changes including early menopause. The risk of being unable to conceive within a year of trying is increased two-



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